pler guidewire. Patients were divided into two groups based on myocardial viability assessed by single-photon emission computed tomographic thallium-201 imaging 6 months after the infarction; 81 patients with viable myocardium and 32 patients with non-viable myocardium. Redistribution patterns or residual maximal myocardial activity >50% are indices of tissue viability.
Results: Coronary flow velocity variables showed significantly higher systolic peak velocity (8±20 vs -31±23 cm/s; p=0.0001) and longer DDT (722±196 vs 312±157 ms; p=0.0001) in viable myocardial group compared with nonviable myocardial group. The optimal cutoff values to predict viable myocardium was 0 cm/s for systolic peak velocity and 600ms for DDT (sensitivity=0.85, specificity=0.94 and sensitivity=0.93, specificity=0.91, respectively).
Conclusion: These data suggest that the CFV pattern is an accurate predictor of the presence or absence of residual myocardial viability at the late stage in patients with anterior AMI.

1157-48 Reduced Shear Stress and Large Shear Stress Gradient Cause Coronary Aneurysm and Thrombus Formation in Children With Kawasaki Disease

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We tested whether reduced shear stress (SS) and large shear stress gradient could be caused coronary artery aneurysm (AN) formation at coronary branching site and thrombus formation in AN in patients with Kawasaki disease (KD). 139 children (2y - 16y) who had coronary abnormality revealed by 2-D echo were subjected. All patients had different sized AN without any significant stenosis in proximal and distal portion of AN and were divided into four groups by the maximum diameter of AN; Group S: < 1.5-fold the diameter of the adjacent normal-looking vessel, n=34, Group M:1.5 </= to < 4.0-fold, n=31, Group L: </= 4.0-hold, n=29, Group N: normal-looking vessels by CAG, n=45. All patients had Aspirin and / or Warfarin. The averaged peak velocity (APV) was measured at the middle of ANs in groups L, M and S, at the branching site of segment 5-6-11 in group N, and at the normal-looking proximal lesion of AN in all 4 groups. SS was calculated by the simplified formula as: shear stress = 4μAPV/(R/2), where μ is blood viscosity, R is maximum inner diameter of AN or coronary vessel. SS gradient was calculated by the formula as: SS gradient = SS at normal-looking lesion / SS at AN or coronary branching site. Also, CAG and IVUS were performed for detection of thrombus and localization of ANs.**Results:*** p < 0.05 vs. groups M, S. SS in normal-looking vessels were 26.6 ± 3.1

	SS in AN or branching site	SS gradient	thrombus
L	6.8+/-3.3*	4.1+/-1.1*	24/29*
M	21.8+/-5.3	1.2+/-0.5	2/31
S	25.6+/-4.6	1.1+/-0.4	0/34
N	9.7+/-2.9*	3.0+/-1.5*	0/45

Conclusions: Reduced shear stress and large shear stress gradient may play a critical role of giant aneurysm and thrombus formation intra coronary aneurysms in Kawasaki disease.

1157-49 Physiologic and Anatomical Evaluation Prior to and After Stent Implantation in Small Coronary Vessels: Final Results of PHANTOM Trial

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Background: Long-term outcomes after PCI of small coronary artery disease remain suboptimal, but there is no diagnostic tool available to define (in)appropriateness of PCI in this setting. This prospective multicenter study investigates the role of intravascular ultrasound (IVUS), quantitative coronary angiography (QCA) and fractional flow reserve (FFR) in patients with small coronary arteries.
Methods: Sixty patients with small coronary arteries (reference diameter <2.8mm) and coronary stenoses between 40-70% were included. A 0.014-in pressure guide wire (Wave Wire) was used for FFR measurements after 2 minutes of IV infusion of adenosine (140 μg/kg/min). Volumetric 3D-IVUS and angiography data were analyzed in an independent core laboratory. PCI was deferred if FFR >0.75. Optimal stenting was defined by IVUS (minimal lumen area (MLA) instent >80% of reference MLA). Clinical follow-up was scheduled at 6 and 12 months.
Results: Mean age was 62.4±10y, 40% had diabetes and 84% had HTN. There were no procedure complications. Mean RD (reference diameter) was 2.1mm. Sixty percent of the patients had normal FFR (<0.75). Seventy percent of patients with a CSA obstruction >70% by IVUS had an FFR<0.75, while 100% with CSA obstruction >75% had FFR <0.75. Angiographic MLD was not correlated with FFR. Forty-four percent had post-stenting FFR<0.90 in spite of optimal IVUS result. Fifty six patients completed at least 6 month follow-up (25 completed 12-month). Among patients who did not undergo index PCI because of an FFR<0.75 (n=27 out of 56 with follow-up), none required follow-up revascularization. There were 5 repeat PCI in the cohort of patients initially treated with PCI (n=23). Complete follow-up data will be presented. **Conclusion:** The majority of intermediate lesions in small vessels may not require PCI. There is a poor correlation between physiological and anatomical parameters in patients with small vessel disease. Deferring PCI based on FFR>0.75 appears to be safe in patients moderate stenosis in small coronary vessels. Considering the high incidence of restenosis, FFR represents a valuable tool to define the appropriateness of PCI in small vessels.

1157-50 Hyperinsulinemia Is Associated With Coronary Endothelial Dysfunction in Obese and Nondiabetic Patients

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Background: The American Heart Association (AHA) has recently classified obesity as a modifiable risk factor for coronary heart disease. Therefore, we evaluated the impact of obesity on insulin resistance and coronary endothelial function in overweight patients with normal or mild coronary artery disease. Methods: A total of 32 consecutive non-diabetic patients with normal or mildly diseased coronary arteries at angiography underwent coronary vascular reactivity evaluation using intracoronary administration of papaverine, acetylcholine and nitroglycerin using a Doppler guidewire. Patients were divided into two groups based on body mass index (BMI): Group 1, patients with a BMI<25 (n = 19, normal weight); and Group 2, patients with a BMI≥25 (n = 13, overweight). The level of fasting immunoreactive insulin (FIRI) and fasting blood glucose (FBS) were measured in each subject. Homeostasis model assessment (HOMA-R) was used as an indicator of insulin resistance. Results: FIRI and HOMA-R in Group 2 were significantly greater than those in Group 1 (4.4±2.7 vs. 14.5±7.4 μU/ml, p<0.01; 1.02±0.62 vs. 3.52±1.77, p<0.01, respectively), whereas FBS was similar when comparing the two groups (95±11 vs. 98±13 mg/dl). The percent change in coronary blood flow and coronary artery diameter induced by acetylcholine in Group 2 had a significant negative correlation with both HOMA-R and FIRI (HOMA-R:r=-0.69, p<0.01; r=-0.64, p<0.02,FIRI: r=-0.69, p<0.01; r=-0.72, p<0.01,respectively) but displayed no significant correlation in Group 1. Conclusions: Obesity with hyperinsulinemia caused by increased insulin resistance is associated with coronary endothelial dysfunction in non-diabetic patients.

POSTER SESSION

1158

Restenosis: Basic Research II

Tuesday, March 09, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1158-51 A Novel Antirestenosis Effect of Paclitaxel-Eluting Stents

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Background: Coronary stenting is a known, potent stimulator of adventitial angiogenesis.These post stent angiogenesis may help neointimal growth and maintenance. Cell migration and proliferation blockage are two known mechanism of Paclitaxel limiting neointimal hiperplasia. Paclitaxel is a known angiogenesis inhibitor in other tissues, like tumors, nonentheless this effect on coronary arteries has not been yet studied. We thus examined adventitial neovascularization in porcine coronary arteries following paclitaxel eluting stent implant and compared them with control stents.
Methods: Forty-three stented arteries, 26 paclitaxel stents (1ug/mm^2) and 17 controls were examined blindly. Adventitial vessels (vasa vasorum) were identified as arterial structures with endothelial cells surrounding a lumen, with or without erythrocytes. Adventitial vessel density was determined by manual counting using a curved geometric shape 400x50 microns placed in the adventitia, bordering the external elastic lamina. Intimal thickness was measured from the back of each strut to the lumen and calculated an average for each artery.
Results: Paclitaxel-stented arteries showed a marked decrease in adventitial vessels compared with control stented vessels (1.5±1.2 versus 3.1 ± 2.2 vessels/20,000 sq microns, p<0.003). There was no statistical difference in minimum intima thickness between the treated and control groups in this mild injury model (paclitaxel: 308.9 ± 57.3, controls: 284.9 ± 59.0 microns, p>0.5).
Conclusions: Paclitaxel elution from stents is associated with markedly decreased adventitial angiogenesis. In addition to its anti migratory and antiproliferative effects, paclitaxel may prevent neointimal growth by preventing adventitial vasa vasorum, limiting oxygen and nutrient supply to the neointima. If true, this opens novel therapeutic strategies for limiting neointimal hyperplasia.

1158-52 Proteomic Profiling of Restenotic Lesions Unveils Increased Expression of Structural Proteins That Are Inhibited by Intramural Delivery of Rapamycin

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Restenosis is the major limiting factor of balloon angioplasty.Identifying genes that regulate neointima formation is ongoing, facilitated by cDNA array profiling of the arterial wall. This study utilizes proteomic profiling to identify gene products involved in arterial remodeling that occurs as a consequence of restenosis. We specifically identified proteins inhibited by rapamycin since this drug is being used clinically for its anti-restenotic properties.
Intramural infusion of rapamycin or its vehicle was delivered through a balloon catheter directly into the vessel wall during angioplasty. After 3 weeks, proteomic profiles of arterial wall segments were obtained. On average, 485 protein spots were consistently

matched between non-dilated and dilated vessels. Differential expression of 12 proteins was observed between the groups and direct sequencing of digested peptides demonstrated that these proteins regulate the structural integrity of the vessel wall. Rapamycin blocked the expression of specific proteins, including lamin A, vimentin, alpha-1-antitrypsin, and alpha-actin. In addition, rapamycin significantly reduced the deposition of elastin, collagen III and fibronectin within the vascular wall. Neointimal formation was likewise decreased and this (0.71±0.1 vs 1.4±0.12 intima-media-ratio, rapamycin vs. vehicle, respectively) could be attributed to the inhibitory properties of rapamycin on ECM deposition and smooth muscle cell proliferation.
Proteomic profiling of restenotic lesions unveils differential expression of structural proteins that regulate vessel wall integrity. Intramural infusion of rapamycin directly to the injured site differentially blocked the expression of these proteins as well as smooth muscle cell proliferation and the deposition of ECM, providing a rationale for the use of rapamycin to prevent unfavorable remodeling of the vascular wall that occurs following angioplasty.

1158-53 Suppressive Effects of Eplerenone on Accumulation of Extra Cellular Matrix in Neointima After Coronary Stent Implantation Using Swine

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Background: Neointimal formation, mainly composed of smooth muscle cell proliferation, is principle cause of restenosis after coronary stent implantation. However increasing evidence suggests that accumulation of extra cellular matrix_including collagen is also an important for neointimal formation. Importance of aldosterone on myocardial fibrosis in heart failure has been reported, but the effects of aldosterone on restenosis after stenting have not been established. We examined the suppressive effects of eplerenone, new type of strong aldosterone receptor antagonist, on the neointimal formation after coronary stenting using swine model. Methods: Palmatz-shatz stent (3.0 mm in diameter) were implanted on the left anterior descending artery for 20 pigs aged 10 weeks weighing from 20 to 25kg.Those were divided for two groups (Group E; oral administration of eplerenone 200 mg/day from 1 week before to 4 weeks after stenting. Group C; oral administration of placebo). Pigs were sacrificed 2 weeks or 4 weeks after stenting. Samples were embedded in paraffin for histological examination. Masson's trichrome staining was used for the assessment of collagen deposition and measurement of %fibrosis area. Anti-α-smooth muscle actin, anti-proliferative cell nuclear antigen (PCNA) and anti-macrophage antibodies were used for immunohistochemical examinations. Results: Newly formed neointima was observed in 2 weeks and was become thicker in 4 weeks. Part of endothelial cells was recovered in 4 weeks in both groups. In neointima, %fibrosis area was significantly smaller in Group E (33.7±15.8 %) than in Group C (40.7±11.8 %)($p<0.05$) in 2 weeks and in Group E (31.3±7.3%) than in Group C (40.4±9.4 %)($p<0.01$) in 4 weeks.Therefore the %area of α-smooth muscle actin was larger in Group E than Group C.Positive staining for PCNA was seen in neointima, especially around stent strut and infiltrating cells including macrophages were mainly observed around stent strut in 2 weeks, but the number of positive cells was similar in both groups. Conclusions: Eplerenone suppresses accumulation of extra cellular matrix in neointima and will be useful to reduce restenosis after coronary stent implantation.

1158-54 Knock-Out of P21 Escapes Radiation-Induced Cell Cycle Arrest and Apoptosis in Vascular Smooth Muscle Cell

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Background: Vascular smooth muscle cell (VSMC) proliferation is important in the pathogenesis of atherosclerosis and restenosis. In spite of delayed catch-up restenosis of intravascular radiation therapy, the biologic mechanism of radiation failure has not been well studied. We investigated the escaping mechanisms of radiation-induced cell cycle arrest and apoptosis
Methods: Using different dosages of gamma radiation, the cell counts, cell cycle, apoptosis, expression and activity of cyclin dependent kinase (CDK), and expression of p16, 21, and 27 were examined with cultured rat and mouse smooth muscle cells.
Results: The cell counts after irradiation with 0, 2, 8, 16 Gray (Gy) (n=9, each) were 3.28, 2.34, 1.94 and 1.30 $x10^5$/ml at 24h, and 5.10, 2.00, 1.80 and 1.20 $x10^5$/ml at 48h, respectively. However, the proportion of apoptosis was minimal, at approximately 10 in 1 $x\ 10^5$ cells. The proportions of cells in the G0/G1, S and G2/M phases were 61, 9 and 30% at 12 hours after 16Gy radiation (control in log phase 61, 34 and 5%), and 67, 7 and 26% (control in confluent phase, 78, 12 and 10%) at 48 hours. By immunoblot analysis and kinase assay, gamma-irradiation with 8 or 16 Gy increased the expression of p21, negative regulator of cell cycle progression, , and decreased the expression and activity of CDK2, an important kinase during the later stages of G1/S progression, as well as the expression and activity of CDK1, which is important in the G2/M phase transition. In contrast, radiation did not affect the expression or activity of either CDK4 or CDK6. The cell-cycle inhibitors, p27 and p16 were not involved in the radiation-induced cell cycle arrest of VSMCs. When p21 knocked out, VSMC proliferation was enhanced, and radiation induced cell cycle arrest and apoptosis were not observed.
Conclusions: Gamma radiation could effectively inhibit VSMC proliferation via cell cycle arrest rather than apoptosis induction, by enhancing p21 expression and suppressing CDK1 and 2. But, the knock-out of p21 escaped antiproliferative effect of radiation. So these findings suggest the degree of p21 expression be the important mechanism of radiation failure and delayed catch-up restenosis.

1158-55 Presence of Mature Dendritic Cells to Early Postangioplasty Neointima: Markers of Antigen Presentation and Anti-Apoptosis

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BACKGROUND – Dendritic cells (DCs) were recently reported following vascular injury. Since information on specific features of DCs during early neointima formation is sparse, we sought to determine characteristics of these cells with respect to DC maturation, survival and antigen presentation.
METHODS – Following rat carotid angioplasty, arterial sections at 7 and 28 days post injury were immunohistochemically examined for S100 and OX-62 as DC markers, CD86 and OX-6 indicating maturation and antigen presentation, Receptor Activator of NF-kB (RANK) whose activation mediates DC survival, and FK506-binding protein 12 (FKBP12), the intracellular receptor of rapamycin.
RESULTS – At day 7 post angioplasty, the majority of neointimal cells were identified as DCs. CD86 and OX-6 labeling were observed in the neointima and the neoadventitia, while DCs remained confined to the neointima. Immunostaining for RANK was consistently found in a pattern similar to DC signaling. Serial sections demonstrated co-expression of FKBP12 exclusively restricted to neointimal DCs. Despite a considerably thicker neointima at day 28, DC markers and RANK were confined to the luminal layer of cells. CD86 and OX-6 also showed a luminal prevalence, while FKBP12 was observed scattered in luminal and deep neointima.
CONCLUSIONS – Mature dendritic cells were the predominant cell type in early neointima, and demonstrated RANK upregulation thought to promote cell survival. Co-expression of FKBP12 and dendritic cell markers suggests that dendritic cells may be considered as principal targets of rapamycin for restenosis prevention.

1158-56 Effects of Wine, Beer, and Whisky on Vascular Endothelium and Thrombosis Fibrinolysis System

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Introduction: Evidence suggests that red wine is associated with decrease cardiovascular risk in general population. It is still unknown whether alcohol or other substances such as bioflavonoids affect endothelial function and thrombosis/fibrinolysis system. We compared the effects of red wine, white wine, beer and whisky on endothelial function and thrombosis/fibrinolysis system.
Methods: The population of the study consisted of 80 healthy young individuals (24±1.6 years old). They were randomised into five equally sized groups and received 264 ml red wine (8 males 8 females), 264 ml white wine (7 males 9 females), 633 ml of beer (7 males 9 females), 79 ml whisky (9 males 7 females), and 250 ml water (8 males 8 females). Forearm blood flow was determined by gauge-strain plethysmography, at baseline, at 1 hour and 4 hours after intake. Endothelium-dependent dilation (EDD) and endothelium independent dilation (EID) were confined as the %change of flow from baseline to the maximum flow during reactive hyperemia or after sublingual nitroglycerin administration respectively. Plasma levels of vonWillebrand factor (vWF) and tissue plasminogen activator (tPA) were determined at baseline at 4 hours after alcohol consumption.
Results: EDD was significantly increased after 1 hour red wine or beer consumption (from 96.6±9.7% and 73.5±8.4% to 125±13.6% and 93.4% respectively, $p<0.05$ for both), while it returned at baseline at 4 hours (100.9±18.8 and 83.7±20.8 respectively, p=NS compared to baseline). EDD remained unchanged in the other groups (p=NS). vWF was decreased in the beer and red wine groups (from 65±4.9 and 62.3±3.7 to 56±4.0% and 56.9±3.9% respectively, $p<0.05$ for both), but not in the other groups. EID and tPA remained unchanged in all groups.
Conclusions: Acute consumption of red wine or beer and not of white wine and whisky increases endothelium-dependent dilation, and decreases vWF levels. These findings indicate that only red wine and beer are associated with improvement of endothelial function and reduced thrombogeneicity.

1158-57 Vascular Access Site Complications Post Percutaneous Coronary Intervention

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Background: Vascular access site complications can occur after percutaneous coronary interventions (PCI). Potential contributing factors include antithrombotic regimens, sheath size, and patient comorbidities. These have evolved significantly over the past decade.
Method: Vascular complications in 16,201 consecutive PCI patients from 1979 to 2002 were assessed using the Mayo Clinic Interventional Registry. The patients were divided into four groups based on PCI procedure date. Group I (1979-1989), N= 3085, balloon angioplasty alone was used in the majority. Group II (1990-1995), N=4753, stent era with vigorous anticoagulation pre and post PCI. Group III (1996-1999), N=4827, antiplatelet agents replaced oral anticoagulation and glycoprotein IIB-IIIA inhibitor use was initiated. Group IV (2000-2002), N=3536, use of clopidogrel along with continued use of Glycoprotein IIB-IIIA agents.
Results: The patients in Group IV were significantly older, had a larger body mass index (BMI), a higher percentage of females, diabetes, hypercholesterolemia, and hypertension compared to the other three groups. Sheath size used in Group IV was significantly smaller (French size) compared to Groups II & III (6.4 +/- 0.8 vs 8.2 +/- 0.7 & 7.8 +/- 0.9 respectively; P<.001). The use of glycoprotein IIB-IIIA inhibitors was significantly greater in Group IV compared to Groups II & III (67% vs 0% & 42% respectively; P<.001). Even